

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-211

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-211

Organon Inc.
Attention: Al Mayo
Executive Director, Regulatory Affairs
375 Mount Pleasant Avenue
West Orange, NJ 07052

Dear Mr. Mayo:

Please refer to your new drug application (NDA) dated January 28, 2000, received January 31, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Follistim[®]-AQ Cartridge (follitropin beta injection).

We acknowledge receipt of your submissions dated January 22, 29, February 13, 24, 26, and March 2, 4, 17(2), 18, and 23 (2), 2004.

The January 22, 2004, submission constituted a complete response to our December 23, 2003, action letter.

This new drug application provides for the use of Follistim[®]-AQ Cartridge (follitropin beta injection) in Assisted Reproductive Technologies (ART).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the attached labeling (package insert, patient package insert, and the Instructions for Use). Immediate container and carton labels must be identical to those attached with the exception that the family logo will be removed at the next printing. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-211.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one marketing package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at (301) 827 - 4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Division Director
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:

21-211

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Organon, Inc.
Attention: Albert Mayo
Vice President, Regulatory Affairs
375 Mt. Pleasant Avenue
West Orange, NJ 07052

Dear Mr. Mayo:

Please refer to your new drug application (NDA) dated January 28, 2000, received January 31, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Follistim[®] -AQ Cartridge (follitropin beta for injection).

We acknowledge receipt of your submissions dated August 5 (2), August 11, and October 31, 2003.

Your October 31, 2003, request for dispute resolution, received on November 3, 2003, concerned the Division's decision to not approve NDA 21-211 under section 505(d) of the Act and 21 CFR 314.125 (b). This appeal was submitted in response to the June 23, 2003, not approvable letter.

The November 24, 2003, response to your request for dispute resolution from Dr. Julie Beitz, Deputy Director of the Office of Drug Evaluation III, informed you of the decision to issue an approvable letter for this application. Therefore, this letter informs you that the application is considered approvable as of June 23, 2003. Before the application may be approved, the following information must be submitted:

1. Draft professional labeling.
2. Draft patient package insert.
3. Plans for an educational program for patients and prescribers focusing on correct use of the pen injector and the need for careful dose conversion when switching from syringe to pen injector or *vice versa*.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.

- Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.
 4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
 5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
 6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
 7. Provide English translations of current approved foreign labeling not previously submitted.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Archana Reddy, M.P.H, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Division Director
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Margaret Kober
12/23/03 11:13:09 AM
signed for Dr. Shames